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Electron-Transfer Reactions of Copper(III)–Peptide Complexes with Tris(1,10-phenanthroline)cobalt(II)

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Tripeptide and tetrapeptide complexes of Cu(III) rapidly oxidize $Co(phen)_3^{2+}$ showing that outer-sphere electron transfer occurs. The rates for reactions between $Co(phen)_3^{2+}$ and ten different uncharged copper(III)–peptide complexes (with $E°$ values for the cross exchange ranging from 0.23 to 0.56 V) exhibit a linear free energy dependence: $\log k_{12} = 0.25$ (± 0.02) $\log K_{12} + 4.4$ (± 0.2). The slope is much less than that predicted by the usual formulation of the Marcus theory. Nevertheless, electron transfer involving copper(III,II)–peptide complexes is shown to be a very facile process.

Introduction

Trivalent copper complexes are formed in aqueous solution by oxidation of copper(II)–deprotonated-peptide complexes[2,3] with $IrCl_6^{2-}$, $S_2O_8^{2-}$, or O_2.[4] Electrochemical oxidation in a flow system also works very well and gives excellent yields.[5-8] The resulting copper(III)–peptide complexes are moderately stable in neutral solution but decompose more rapidly in either acidic or basic solutions.[7,9] The electrode potentials for $Cu^{III,II}$(peptide) couples are very sensitive to changes in the nature of the ligand[10] and span a range from 0.45 to 1.02 V.[3]

The rate of reaction between $Ir^{IV}Cl_6^{2-}$ and $Cu^{II}(H_{-3}G_4)^{2-}$ is too rapid to be measured by normal stopped-flow methods. However, the reverse reaction (eq 1) has been studied where

$$Cu^{III}(H_{-3}G_4)^- + Ir^{III}Cl_6^{3-} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Cu^{II}(H_{-3}G_4)^{2-} + Ir^{IV}Cl_6^{2-} \qquad (1)$$

acid dissociation of the $Cu^{II}(H_{-3}G_4)^{2-}$ complex (eq 2) forced

$$Cu^{II}(H_{-3}G_4)^{2-} + \text{acid} \xrightarrow{\text{rapid}} Cu^{2+} + HG_4 \qquad (2)$$

the redox reaction. Under the conditions used the uphill electron-transfer reaction ($k_1 = 1.0 \times 10^4$ M^{-1} s^{-1}) was the rate-limiting step.[11] Knowledge of the self-exchange kinetics for $IrCl_6^{2-}$ and $IrCl_6^{3-}$ ($k_{11} = 2.3 \times 10^5$ M^{-1} s^{-1} at 0.1 M $NaClO_4$, 25.0 °C)[12] permits the calculation of the self-exchange rate constant (k_{22}) for $Cu^{III,II}(H_{-3}G_4)^{1-,2-}$, provided that the reactions are outer-sphere electron-transfer processes and that the Marcus theory[13] is applicable. For the triply depronated G_4 complex, k_{22} is 4×10^7 M^{-1} s^{-1}. The velocity of the electron-transfer reaction of other copper(III,II)–peptide complexes is impressive. A k_{22} value of 7×10^7 M^{-1} s^{-1} is calculated from the reactions of the neutral copper(III)–peptide complexes with $IrCl_6^{3-}$ which fit the Marcus correlation.[11] Thus, the copper(III,II)–peptide complexes are in a select group of species having very fast self-exchange processes. The efficiency of the Cu(II), Cu(III) electron transfer is evidenced by the role of $Cu^{III}(H_{-3}G_4)^-$ as a redox catalyst in oxygen uptake by $Cu^{II}(H_{-3}G_4)^{2-}$.[7] The speed of these electron-transfer processes also enhances the feasibility of Cu(III) intermediates in biologically important oxidation–reduction reactions involving copper.

In the present study the rates of reaction of a number of copper(III)–peptide complexes with tris(1,10-phenanthroline)cobalt(II) are measured (eq 3). The $E°$ value for

$$Cu^{III}(\text{peptide})^{0,1-} + Co^{II}(phen)_3^{2+} \xrightarrow{k_{12}} Cu^{II}(\text{peptide})^{1-,2-} + Co^{III}(phen)_3^{3+} \qquad (3)$$

$Co(phen)_3^{3+,2+}$ is 0.38 V,[14] so the cross exchange reactions are thermodynamically favorable ($E°$ values of +0.13 to +0.56 V depending on the peptide). The self-exchange reaction for the $Co(phen)_3^{3+,2+}$ couple has been examined in some detail by Baker, Basolo, and Neumann.[15] In their study a value of $\sim$6 M^{-1} s^{-1} was obtained for the exchange rate constant at 0 °C and 0.1 M KNO_3. Activation parameters were obtained from a temperature dependence; however, no electrolyte was employed. Hence, use of the exchange rate at 25 °C calculated from these parameters is of doubtful validity in the present study where $\mu = 0.1$ M. A self-exchange rate constant of $\sim$40 M^{-1} s^{-1} can be calculated for this couple at 25 °C and 0.1 M KNO_3 by using activation parameters determined by Neumann cited in Farina and Wilkins.[16] However, a direct experimental determination of the self-exchange rate as 14 M^{-1} s^{-1} (25 °C, 0.05 M NaCl) by Brückner, Crescenzi, and Quadrifoglio[17] is employed in the present work.

In the previous work where $IrCl_6^{3-}$ was used to reduce the copper(III)–peptides, a weak chloride bridge between iridium and the square-planar copper complexes could not be ruled out. The redox rate for the reaction in eq 3 is much faster than the substitution rates of $Co(phen)_3^{2+}$ or of the coordinated peptides of copper(III). The axial substitution characteristics of copper(III) are not known; however, for eq 3 there are no bridging ligands which can coordinate between the metal atoms. Hence, this system was selected to provide a test of the speed of the outer-sphere self-exchange reactions of $Cu^{III,II}$(peptide) systems.

Experimental Section

Reagents. Tris(1,10-phenanthroline)cobalt(II) perchlorate was prepared[15,18,19] by mixing aqueous solutions of 1,10-phenanthroline monohydrate and $CoSO_4 \cdot 7H_2O$ in a 3.2:1 mole ratio and then adding $NaClO_4$ to precipitate $[Co(phen)_3](ClO_4)_2 \cdot H_2O$. The molar absorptivities of $Co(phen)_3^{2+}$ at 400 nm (ϵ 200 M^{-1} cm^{-1}) and at 375 nm (ϵ 478 M^{-1} cm^{-1}) agreed with those reported by Ellis and Wilkins.[20] The cobalt(III) complex, $[Co(phen)_3](ClO_4)_3 \cdot 2H_2O$, also was prepared[15] and its molar absorptivities agreed with those reported previously (450 nm, ϵ 99 M^{-1} cm^{-1}; 350 nm, ϵ 3700 M^{-1} cm^{-1}; 330 nm, ϵ 4680 M^{-1} cm^{-1}).[19]

The oligopeptides were obtained as chromatographically pure substances and were used without further purification. A $Cu(ClO_4)_2$ solution was prepared and standardized by EDTA titration. The copper(II)–peptide complexes (6×10^{-4} M) were prepared with excess peptide (typically 25% mole excess) and adjusted to pH 9 in the case of the tripeptides and to pH 10–11.5 in the case of the tetrapeptides and tripeptide amides in the presence of 0.05 M NaCl. The copper(III)–peptide solutions were prepared by electrochemical oxidation with a flow system in which the electrode arrangement included a graphite powder working electrode packed in a porous glass column, wrapped externally with a platinum wire electrode.[21] After electrolysis the copper(III)–peptide solutions were approximately neutral and were diluted to $\leq 1 \times 10^{-5}$ M by using acetate buffer containing sufficient NaCl to give an ionic strength of 0.10 M.

Kinetic Measurements. The rates of the oxidation–reduction reactions were measured with a Durrum stopped-flow spectrometer interfaced to a Hewlett-Packard Model 2115A general purpose computer.[22] In each case, freshly prepared solutions of copper(III) were used. Cobalt(II) solutions ($\lesssim 2.5 \times 10^{-4}$ M) were prepared daily by dissolution of $Co(phen)_3(ClO_4)_2 \cdot H_2O$. The ionic strength of the cobalt(II) solutions was adjusted to 0.1 M by using a standard sodium chloride solution. Solid 1,10-phenanthroline monohydrate was added to give 20% molar excess of phenanthroline which was required to

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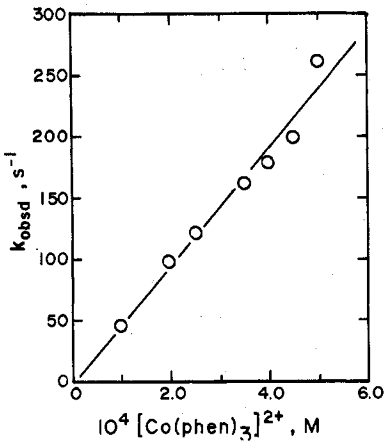

Figure 1. Dependence of the observed first-order rate constant for the loss of $Cu^{III}(H_{-3}G_4)^-$ upon concentration of $Co(phen)_3^{2+}$, 25.0 °C, $\mu = 0.1$ M (NaCl + NaOAc), pH 5.4, with 18% excess phen in solution. The least-squares fit gives a slope of $4.8\ (\pm 0.4) \times 10^5\ M^{-1}\ s^{-1}$ for the second-order rate constant.

Table I. Variation of the Pseudo-First-Order Rate Constant with $Co(phen)_3^{2+}$ for the Reaction with $Cu^{III}(H_{-3}$prolylglycylglycinamide$)^a$

$10^5\ [Co^{II}(phen)_3^{2+}]$, M	$10^5\ [Cu^{III}(H_{-3}PGGa)]$, M	k_{obsd}, s^{-1}	$10^{-5}k_{12}$,^{b} $M^{-1}\ s^{-1}$
3.23	0.36	7.6	2.4
6.45	0.72	10.4	1.6
12.9	1.2	22.7	1.8
19.9	1.2	32.3	1.6
39.8	1.2	73.9	1.9

^{a} At 25.0 °C, $\mu = 0.1$ M (NaCl), $[acetate]_T = 0.005$ M, pH 5.35. ^{b} Average $k_{12} = (1.9 \pm 0.3) \times 10^5\ M^{-1}\ s^{-1}$.

eliminate the presence of a small (~4%) portion of bis(1,10-phenanthroline)cobalt(II). The reactivity of the copper(III)–peptides with 1,10-phenanthroline also was tested with $Cu^{III}(H_{-3}G_4)^-$ and $Cu^{III}(H_{-2}G_2\beta A)$ and was shown to be negligible under the conditions employed in this study.

The electron-transfer reactions (25.0 °C) were followed for at least 3 half-lives by monitoring the disappearance of the intense charge-transfer band of copper(III) occurring at 365 nm ($\epsilon \simeq 7000\ M^{-1}\ cm^{-1}$) for the tetrapeptides and tripeptide amides and at 390 nm ($\epsilon \sim 5000\ M^{-1}\ cm^{-1}$) for the tripeptides. Absorbance vs. time data were collected and ensembled for three kinetic runs. The data for each set of runs were subjected to linear and nonlinear regression analyses which gave the values of pseudo-first-order rate constant (k_{obsd}), initial absorbance (A_0), and final absorbance (A_∞) described by eq 4 and 5.

$$\ln (A - A_\infty) = -k_{obsd}t + \ln (A_0 - A_\infty) \qquad (4)$$

$$-d[Cu^{III}(H_{-n}L)]/dt = k_{obsd}[Cu^{III}(H_{-n}L)] \qquad (5)$$

Results and Discussion

At least a tenfold excess of tris(1,10-phenanthroline)cobalt(II) was present in each kinetic run. Under these conditions, excellent first-order plots were obtained. Thus, the reactions were shown to be first order with respect to the copper(III) species. The order of reaction with respect to cobalt(II) was examined by using excess $Co(phen)_3^{2+}$ with $Cu^{III}(H_{-3}G_4)^-$ (Figure 1) and with $Cu^{III}(H_{-3}PGGa)$ (Table I). A linear variation of k_{obsd} with [Co(II)] was obtained in both cases showing that the reactions also are first order with respect to [Co(II)].

Attempts to prepare 1.0×10^{-4} M solutions of $Co(phen)_3^{2+}$ in 0.2, 0.1, and 0.01 M $NaClO_4$ failed due to precipitation of the perchlorate salt. Thus, sodium chloride was chosen to be the supporting electrolyte. The effect of increasing chloride concentration was examined by using reactions of $Cu^{III}(H_{-3}G_4)^-$ with $Co(phen)_3^{2+}$ (Table II). Increasing sodium chloride concentration and simultaneously increasing ionic strength had relatively little effect on the second-order rate constant.

Table II. Effects of Increasing Chloride Ion Concentration and Simultaneously Increasing Ionic Strength upon the Rate of the Reaction of Tris(1,10-phenanthroline)cobalt(II) with Copper(III) Tetraglycine^a

$[Cl^-]$, M	μ, M	k_{12}, $M^{-1}\ s^{-1}$
0	0.0046	6.44×10^5
0.046	0.050	5.96×10^5
0.496	0.50	5.40×10^5
0.996	1.00	5.58×10^5

^{a} At 25 °C, $[acetate]_T = 0.05$, and pH 3.78.

Table III. Kinetic Data for the Reactions of Uncharged Cu(III)–Peptide Complexes and $Cu^{III}(H_{-3}G_5)^-$ with $Co(phen)_3^{2+}$ (25.0 °C, $\mu = 0.1$ M (NaCl–NaOAc))

copper(III) complex	$10^4[Co(phen)_3^{2+}]$, M	pH	k_{obsd}, s^{-1}	$10^{-5}k_{12}$, $M^{-1}\ s^{-1}$
$Cu^{III}(H_{-3}PG_2a)^a$	1.29	4.74	23.6	1.83
		5.36	22.7	1.76
		5.79	22.7	1.76
		6.43	23.5	1.82
$Cu^{III}(H_{-3}G_3a)^a$	1.25	5.03	26.4	2.16
		5.09	27.3	2.19
		5.15	28.1	2.26
		5.29	26.1	2.14
		5.50	25.9	2.12
		5.78	26.3	2.16
$Cu^{III}(H_{-3}G_4a)^b$	0.828	5.06	46.6	5.63
		5.26	47.8	5.77
		5.46	46.4	5.60
$Cu^{III}(H_{-3}G_3AOCH_3)^a$	1.35	4.77	137	10.1
		5.44	135	9.98
		5.82	135	9.98
		5.91	134	9.90
$Cu^{III}(H_{-2}L_3)^a$	1.26	5.90	101	8.04
$Cu^{III}(H_{-2}A_3)^b$	0.828	5.06	145	17.5
		5.26	151	18.2
		5.44	150	18.1
$Cu^{III}(H_{-2}GA_2)^b$	0.846	5.06	193	22.8
		5.28	186	22.0
		5.49	181	21.4
$Cu^{III}(H_{-2}G_2A)^b$	0.730	4.74	259	35.5
		5.04	250	34.2
		5.34	271	37.1
$Cu^{III}(H_{-2}G_3)^b$	0.846	5.06	360	42.6
		5.30	307	36.3
		5.47	380	44.9
$Cu^{III}(H_{-2}G_2\beta A)^b$	0.846	5.06	404	47.8
		5.28	471	55.7
		5.49	459	54.2
$Cu^{III}(H_{-3}G_5)^{-\,b}$	0.828	5.06	56.9	6.87
		5.26	57.6	6.96
		5.44	57.0	6.88

^{a} $[Acetate]_T = 0.005$ M. ^{b} $[Acetate]_T = 0.05$ M.

The rate constants for the reactions of $Co(phen)_3^{2+}$ with the uncharged copper(III)–peptide complexes and with $Cu^{III}(H_{-3}G_5)^-$ are independent of hydrogen ion concentration as shown in Table III. The lack of a hydrogen ion dependence in this pH region is expected for the copper(III)–tripeptides and tripeptide amides since they should not undergo appreciable protonation above pH ~3 by analogy with $Ni^{II}(H_{-2}G_3)^-$ [23] and $Ni^{II}(H_{-3}G_3a)^-$.[24] Lack of a hydrogen ion dependence for $Cu^{III}(H_{-3}G_5)^-$ is also expected because its outside protonated species is less stabilized by internal hydrogen bonding than the corresponding copper(III)–tetrapeptide complexes.[24,25]

On the other hand, rate constants for the copper(III)–tetrapeptide complexes, $Cu^{III}(H_{-3}G_4)^-$, $Cu^{III}(H_{-3}A_4)^-$, and

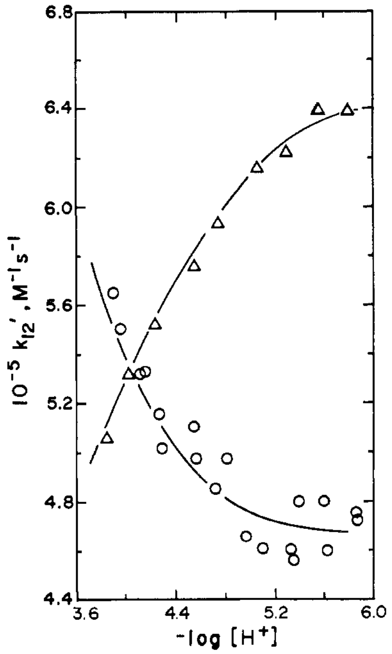

Figure 2. Acid dependence of the second-order rate constants for reaction of negatively charged copper(III)–peptide complexes with $\mathrm{Co(phen)_3^{2+}}$ (○, $\mathrm{Cu^{III}(H_{-3}G_4)^-}$; △, $\mathrm{Cu^{III}(H_{-3}A_4)^-}$) at 25.0 °C and μ = 0.1 M. The solid lines fit eq 7 with values for k_{12}, k_{12}^{H}, and K_{H} of 4.6×10^5 M^{-1} s^{-1}, 6×10^5 M^{-1} s^{-1}, and 1×10^4 M^{-1}, respectively, for $\mathrm{Cu^{III}(H_{-3}G_4)^-}$ and 6.4×10^5 M^{-1} s^{-1}, 5×10^5 M^{-1} s^{-1}, and 2×10^4 M^{-1}, respectively, for $\mathrm{Cu^{III}(H_{-3}A_4)^-}$.

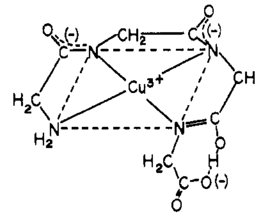

Figure 3. Proposed structure for the outside protonation of the copper(III)–tetraglycine complex to give $\mathrm{Cu^{III}(H_{-3}G_4)H}$.

$\mathrm{Cu^{III}(H_{-3}V_4)^-}$, vary in different ways with pH. As shown in Table IV, the rate constant obtained with $\mathrm{Cu^{III}(H_{-3}G_4)^-}$ increased by 25% as the pH decreased from 6.0 to 4.0, whereas that obtained with $\mathrm{Cu^{III}(H_{-3}A_4)^-}$ decreased by 25% through the same change in pH (Figure 2). Under similar conditions, the $\mathrm{Cu^{III}(H_{-3}V_4)^-}$ rate constant was almost independent of pH.

The pH effect with the tetrapeptide complexes can be attributed to "outside" protonation, in which the metal-deprotonated peptide bonds are kept intact but the peptide oxygen is protonated. This has been observed in the crystal structure of the protonated bis(glycylglycinato)cobaltate(III) complex.[26] It also is postulated that nickel(II)–tetraglycine[24] and copper(II)–glycylglycylhistidine complexes[25] undergo outside protonation at pH 4. A similar situation in which a proton can add to the peptide oxygen assisted by hydrogen bonding to the free carboxylate group is shown in Figure 3 for $\mathrm{Cu^{III}(H_{-3}G_4)H}$. Copper(III)–peptide complexes without the free carboxylate group would not be expected to add outside protons before pH 2–3, as is the case for nickel(II)–triglycinamide.[24]

Outside protonation has the obvious effect of converting the copper(III)–tetrapeptide complexes to neutral species which would be expected to diminish the k_{12} values because of the loss of favorable electrostatic interaction with $\mathrm{Co(phen)_3^{2+}}$. However, an opposing effect is expected because the protonated copper(III)–tetrapeptide complexes should have increased oxidizing power. Outside protonation is known to weaken metal–N(peptide) bonds as shown by the crystal structure determination[26] and by the increased kinetic reactivity of nickel(II) and copper(II) complexes.[24,25] The copper(II)–peptide $E°$ values are sensitive to the nature of the coordinated ligand and $E°$ increases as deprotonated peptide groups are replaced by other ligands.[3] Hence, the outside protonated species should have more positive $E°$ values, which would tend to increase the electron-transfer rate. Apparently these opposing factors cancel one another for the $\mathrm{Cu^{III}(H_{-3}V_4)^-}$ reaction and have small, but different, effects for the $\mathrm{Cu^{III}(H_{-3}G_4)^-}$ and $\mathrm{Cu^{III}(H_{-3}A_4)^-}$ reactions with $\mathrm{Co(phen)_3^{2+}}$.

Table IV. Kinetic Data for the Reactions of Negatively Charged Copper(III)–Peptide Complexes with $\mathrm{Co(phen)_3^{2+}}$ (25.0 °C, μ = 0.1 M (NaCl–NaOAc))

copper(III) complex	$10^4[\mathrm{Co(phen)_3^{2+}}]$, M	pH	k_{obsd}, s^{-1}	$10^{-5}k_{12}$, M^{-1} s^{-1}
$\mathrm{Cu^{III}(H_{-3}G_4)^{-}}$ [a]	1.20	3.91	68.2	5.66
		3.96	66.3	5.50
		4.11	64.0	5.33
		4.12	64.3	5.34
		4.28	61.8	5.15
		4.31	60.5	5.02
		4.55	61.2	5.10
		4.56	59.9	4.98
		4.64	59.2	4.92
		4.82	60.9	5.08
		4.88	56.2	4.66
		5.11	50.6	4.22
		5.15	55.7	4.62
		5.32	55.6	4.63
		5.35	54.6	4.54
		5.58	59.5	4.79
		5.61	55.1	4.58
		5.87	57.2	4.74
		5.88	56.4	4.70
$\mathrm{Cu^{III}(H_{-3}A_4)^{-}}$ [a]	1.25	3.84	63.3	5.06
		4.04	66.8	5.34
		4.27	69.3	5.54
$\mathrm{Cu^{III}(H_{-3}A_4)^{-}}$ [a]	1.25	4.53	72.3	5.78
		4.76	74.3	5.94
		5.03	77.8	6.22
		5.31	78.1	6.25
		5.57	80.2	6.42
		5.82	79.9	6.38
$\mathrm{Cu^{III}(H_{-3}V_4)^{-}}$	0.725	5.00[b]	16.6	2.29
		5.48[b]	16.0	2.21
	1.02	4.71[b]	24.7	2.42
		5.36[b]	25.2	2.47
		5.51[a]	24.7	2.42

[a] $[\mathrm{HOAc}]_{\mathrm{T}} = 0.005$ M. [b] $[\mathrm{HOAc}]_{\mathrm{T}} = 0.05$ M.

The data obtained for the pH effect on the copper(III)–tetraglycine reaction with $\mathrm{Co(phen)_3^{2+}}$ were analyzed in terms of the reaction mechanism proposed in the $\mathrm{IrCl_6^{3-}}$ study (eq 6).[11] This leads to the expression for the observed first-order rate constant given in eq 7. The values of k_{12}, k_{12}^{H}, and K_{H} obtained from a nonlinear regression analysis of the data are 4.7×10^5 M^{-1} s^{-1}, 7×10^5 M^{-1} s^{-1}, and 5 (±5) $\times 10^3$ M^{-1}, respectively. If the K_{H} value of 1×10^4 obtained from a similar resolution of data for copper(III)–tetraglycine and hexa-

$$\begin{array}{l} \mathrm{Cu^{III}(H_{-3}G_4)^-} + \mathrm{Co(phen)_3^{2+}} \xrightarrow{k_{12}} \text{products} \\ \quad + \\ \quad \mathrm{H^+} \\ K_{\mathrm{H}} \downarrow\uparrow \\ \mathrm{Cu^{III}(H_{-3}G_4)H} + \mathrm{Co(phen)_3^{2+}} \xrightarrow{k_{12}^{\mathrm{H}}} \text{products} \end{array} \qquad (6)$$

$$k_{\mathrm{obsd}} = \left[\frac{k_{12} + k_{12}^{\mathrm{H}} K_{\mathrm{H}}[\mathrm{H^+}]}{1 + K_{\mathrm{H}}[\mathrm{H^+}]} \right] [\mathrm{Co(phen)_3^{2+}}] \qquad (7)$$

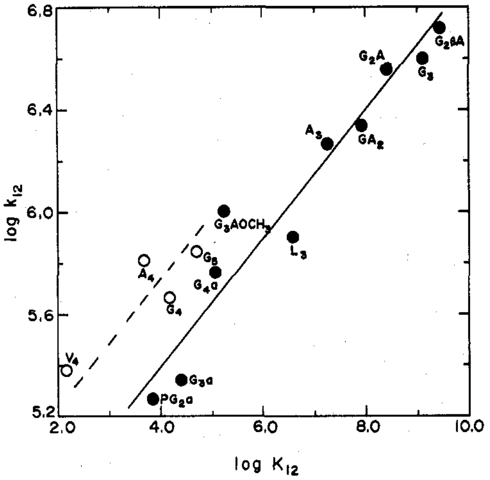

Figure 4. Free energy dependence of the electron-transfer rate constants of copper(III)–peptides with $Co(phen)_3^{2+}$: ○, uninegatively charged Cu(III) complexes; ●, uncharged Cu(III) complexes. The least-squares slope for the solid line is 0.25 (±0.02) and the intercept is 4.4 (±0.2).

chloroiridate(III) is used, the fit is also acceptable and gives values of 4.6×10^5 M^{-1} s^{-1} and 6×10^5 M^{-1} s^{-1} for k_{12} and $k_{12}{}^{H}$. The latter fit is preferred because the larger relative change in rate constant with pH in the Cu(III)–Ir(III) study makes its value for K_H more reliable.

It should be emphasized that the effect of $[H^+]$ on the rate constants for the copper(III)–tetraglycine reaction with $IrCl_6^{3-}$ is much greater than for the reaction with $Co(phen)_3^{2+}$. In the $IrCl_6^{3-}$ reactions, protonation to form $Cu^{III}(H_{-3}G_4)H^0$ gives electrostatically more favorable reactants as well as thermodynamically more favorable $E°$ values. As a result of the effects operating in the same direction, all the copper(III)–tetrapeptides react faster with $IrCl_6^{3-}$ as the acidity increases. This is in contrast to the behavior in Figure 2 where increased hydrogen ion concentration causes relatively small changes and the direction of the change varies from one tetrapeptide complex to another.

For comparison of the rate behavior of the different copper(III)–peptides, rate constants for the copper(III)–tetrapeptides were taken from the plateau of values above pH 5.4, avoiding any effects of outside protonation of the peptide complexes. The resulting k_{12} constants obtained in this study are summarized in Table V. Figure 4 shows the variation in the rate constant for these reactions as a function of the driving force. For the reaction of the neutral copper(III)–peptides with $Co(phen)_3^{2+}$ a least-squares analysis of the data yields eq 8.

$$\log k_{12} = 0.25\ (\pm 0.02) \log K_{12} + 4.4\ (\pm 0.2) \qquad (8)$$

A similar tendency is exhibited by the reaction of the uninegative copper(III)–peptides with $Co(phen)_3^{2+}$. This parallel behavior is represented by the dashed line in Figure 4. In general, the reactions of the uninegatively charged Cu(III) complexes are faster than those involving the uncharged complexes due to the electrostatic attraction between the 1– and 2+ charged reactants. Application of simple Debye–Hückel theory suggests an increase in rate of ~0.5 log unit might be expected for these charge types at 0.1 M ionic strength. This is in qualitative agreement with the increase in rate observed in Figure 4.

Table V. Summary of Rate Constants Obtained for the Reactions of Various Copper(III)–Peptide Complexes with Tris(1,10-phenanthroline)cobalt(II) (at 25.0 °C, $\mu = 0.1$ M (NaCl–NaOAc))

copper(III) complex	$E°$, $V^{a,b}$	k_{12}, M^{-1} s^{-1}
$Cu^{III}(H_{-3}V_4)^-$	0.13	2.4×10^5
$Cu^{III}(H_{-3}A_4)^-$	0.22	6.4×10^5
$Cu^{III}(H_{-3}PG_2a)$	0.23	1.8×10^5
$Cu^{III}(H_{-3}G_4)^-$	0.25	4.6×10^5
$Cu^{III}(H_{-3}G_3a)$	0.26	2.2×10^5
$Cu^{III}(H_{-3}G_5)^-$	0.28	6.9×10^5
$Cu^{III}(H_{-3}G_4a)$	0.30	5.7×10^5
$Cu^{III}(H_{-3}G_3AOCH_3)$	0.31	1.0×10^6
$Cu^{III}(H_{-2}L_3)$	0.39	8.0×10^5
$Cu^{III}(H_{-2}A_3)$	0.43	1.8×10^6
$Cu^{III}(H_{-2}GA_2)$	0.47	2.2×10^6
$Cu^{III}(H_{-2}G_2A)$	0.50	3.6×10^6
$Cu^{III}(H_{-2}G_3)$	0.54	4.0×10^6
$Cu^{III}(H_{-2}G_2\beta A)$	0.56	5.2×10^6

[a] The $E°$ values are for the cross reactions between Cu(III) and Co(II). [b] The potential for the $Co(phen)_3^{3+}$–$Co(phen)_3^{2+}$ couple was calculated to be 0.38 V (25 °C, $[KNO_3] = 0.10$ M) by using data from ref 14. The potentials for the copper(III)–peptides are from ref 3 except for $Cu^{III}(H_{-2}PG_2a)$ and $Cu^{III}(H_{-3}G_3AOCH_3)$ which are from ref 11.

An attempt was made to apply the Marcus theory[13] for outer-sphere electron transfer as formulated in eq 9 and 10

$$k_{12} = (k_{11}k_{22}K_{12}f)^{1/2} \qquad (9)$$

$$\log f = (\log K_{12})^2/4 \log (k_{11}k_{22}/Z) \qquad (10)$$

to the reduction reactions of the uncharged copper(III) complexes where the electrostatic attraction of the reactants is unimportant. The k_{12} values were taken from Table V, $k_{11} = 14$ M^{-1} s^{-1},[17] K_{12} was computed from the $E°$ values in Table V, and $Z = 10^{11}$ M^{-1} s^{-1}. Initially f was set equal to 1 and a value for the Cu(III,II) self-exchange, k_{22}, was computed. This initial estimate of k_{22} was then used in eq 10 to calculate f. The initial value of f was then introduced back into eq 9 to compute a new k_{22}. This iterative procedure was continued until constant values for k_{22} and f were obtained for each pair of reactants. The f values ranged from 0.56 to 0.045 for $Cu^{III}(PG_2a)$ and $Cu^{III}(G_2\beta A)$, respectively. The standard Marcus correlation plot of $\log (k_{12}/f^{1/2})$ vs. $\log K_{12}$ yielded the relationship in eq 11. The value of the slope in eq 11 is

$$\log (k_{12}/f^{1/2}) = 0.34\ (\pm 0.02) \log K_{12} + 4.1\ (\pm 0.2) \qquad (11)$$

well below the slope of 0.5 predicted by eq 9.

The $Co(phen)_3^{2+}$ reductant appears to be responsible for this peculiar behavior since reductions of these uncharged copper(III)–peptide complexes by $IrCl_6^{3-}$,[11] (2,9-dimethyl-1,10-phenanthroline)copper(I),[27] and nickel(II)–peptide complexes[28] all show Marcus type free energy correlations with slopes of 0.5 within experimental error. The latter linear free energy correlations also suggest that there is little change in the Cu(II,III) self-exchange rate as the substituents on the peptide chains are varied and as the atoms coordinating the metal vary from four nitrogens (tetrapeptides and tripeptide amides) to three nitrogens and an oxygen (tripeptides).

Free energy dependences with a slope of other than the 0.5 predicted by eq 9 are not uncommon for reactions involving the Co(II,III) couple. Farina and Wilkins[16] observed a smaller variation of $\log k_{12}$ with free energy than that predicted by eq 9 when $Co(terpy)_2^{2+}$ was oxidized by a number of other cobalt complexes. Przystas and Sutin[19] observed that the rate of oxidation of $Co(phen)_3^{2+}$ by Fe^{3+} and the rates of reduction of $Co(phen)_3^{3+}$ by Cr^{2+} and V^{2+} were all lower than the rates predicted with the Marcus theory. McArdle, Yocom, and Gray[29] have reported rates for the oxidation of $Co(terpy)_2^{2+}$ and $Ru(NH_3)_5py^{2+}$ by several substituted tris(1,10-phenanthroline)cobalt(III) complexes which show marked deviation from eq 9 and 10. Finally, Rillema and Endicott[30] have examined the oxidation of Co^{II}(TIM) and Co^{II}(trans[14]diene) (macrocyclic ligands with four nitrogen donors) by tris(1,10-phenanthroline) and tris(bipyridyl) complexes of iron(III) and ruthenium(III). In this study the relationship

$\Delta G^{\ddagger}_{21} = a_{21} + 0.33\Delta G^{\circ}_{21}$ was observed for the oxidation of the Co(II) complexes.

As yet there has not been a satisfactory explanation which accounts for this peculiar behavior of the Co(II,III) couple. Bodek and Davies[31] have applied Rosseinsky's[32] modification of eq 9 to account for the behavior of redox reactions of aquocobalt(III). However, Rillema and Endicott[30] indicate that the Rosseinsky expression predicts a stronger dependence of k_{12} on self-exchange rate constants than is observed for the Co(II) complexes they studied. Przystas and Sutin[19] argue that a spin multiplicity change in going from $Co(phen)_3^{2+}$ ($t_{2g}^5e_g^2$) to $Co(phen)_3^{3+}$ (t_{2g}^6) does not satisfactorily account for its peculiar behavior. They postulate the production of a radical ion intermediate with the electron in the π system of the phenanthroline ligand as the initial product of $Co(phen)_3^{3+}$ reductions. However, in a later work Chou, Creutz, and Sutin[33] apparently ignore the previously suggested radical ion intermediate and peculiarities associated with the $Co(phen)_3^{3+,2+}$ couple.

The unusual free energy dependence exhibited by the reactions considered in the present work suggests that application of the Marcus theory to cross reactions that involve Co(II) complexes may not be valid when there is an appreciable free energy change. The form of the linear free energy relationship as given in eq 8 suggests that the application of other formulations of the Marcus theory might be more useful in explaining the observed behavior. Equation 8 appears to be consistent with the expression derived for strong overlap electron transfer[34] as given in eq 12. If this application is valid,

$$k_{12} \simeq (k_{11}k_{22}K_{12}^{1+c})^{1/2} \tag{12}$$

then the intercept of Figure 4 where $K_{12} = 1$ and $k_{12} = (k_{11}k_{22})^{1/2}$ yields a value of 5×10^7 M^{-1} s^{-1} (25 °C, 0.1 M NaCl) for the self-exchange rate constant for the uncharged Cu(III) complexes. This self-exchange rate constant is in good agreement with the value of 7×10^7 M^{-1} s^{-1} obtained for the same Cu(III) complexes when $IrCl_6^{3-}$ was the reductant.[11] However, the "strong overlap" designation seems inappropriate for reactions involving $Co(phen)_3^{2+}$ since there are no bridging ligands which can coordinate between the metal atoms. The strong overlap formulation in eq 12 has been invoked in cases where evidence of inner-sphere behavior exists.[35]

An alternate approach using the form of the Marcus equation advanced by Rosseinsky,[32] eq 13, also allows a

$$k_{12} = k_{11}^{\alpha}k_{22}^{1-\alpha}K_{12}^{\alpha} \tag{13}$$

calculation of the self-exchange rate for the copper(III) peptides, where $\alpha = 0.25$ and $k_{22} = 3 \times 10^5$ M^{-1} s^{-1}. It is not possible from this study to determine if either of these treatments is correct. It is evident, however, that electron transfer involving copper(III,II)–peptide complexes is a very facile process.

Conclusions

Copper(III)–peptide complexes participate in very rapid outer-sphere electron-transfer reactions with $Co(phen)_3^{2+}$. The rate of these reactions shows a linear dependence on free energy; however, the slope of the free energy dependence is significantly lower than the 0.5 value predicted by the commonly employed formulation of Marcus theory. The characteristics of the free-energy dependence show qualitative agreement with that observed by Rillema and Endicott[30] for the oxidation of several other Co(II) complexes.

The peculiar free energy correlations observed in this study and others where Co(II) complexes are the reductant suggest that application of Marcus theory to redox processes involving Co(II) may not be valid in all cases. In particular, calculation of the self-exchange rate for an oxidant from a single cross exchange reaction where a Co(II) complex is the reductant is suspect if the free energy change for the reaction is large.

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Registry No. $Cu^{III}(H_{-3}V_4)^-$, 62959-93-7; $Cu^{III}(H_{-3}A_4)^-$, 68628-66-0; $Cu^{III}(H_{-3}PG_2a)$, 24212-63-3; $Cu^{III}(H_{-3}G_4)^-$, 57692-61-2; $Cu^{III}(H_{-3}G_3a)$, 62801-36-9; $Cu^{III}(H_{-3}G_5)^-$, 68550-43-6; $Cu^{III}(H_{-3}G_4a)$, 68550-44-7; $Cu^{III}(H_{-3}G_3AOCH_8)$, 69042-73-5; $Cu^{III}(H_{-2}L_3)$, 69042-72-4; $Cu^{III}(H_{-2}A_3)$, 69042-71-3; $Cu^{III}(H_{-2}GA_2)$, 69814-92-2; $Cu^{III}(H_{-2}G_2A)$, 69814-93-3; $Cu^{III}(H_{-2}G_3)$, 69814-94-4; $Cu^{III}(H_{-2}G_2\beta A)$, 69814-95-5; $Co(phen)_3^{2+}$, 16788-34-4.

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